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DOI: https://doi.org/10.1515/ijamh-2013-0330

DOI 10.1515/ijamh-2013-0330 — Int J Adolesc Med Health 2014; 26(4): 525–530

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Keywords: depression; illicit street drug; mental health; non-medical use of prescription drug.

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Introduction

Prescription drugs are fundamental to the treatment of pain and psychiatric disorders such as depression or anxiety. Unfortunately, they can also cause abuse and dependency (1, 2), and this kind of use constitutes a critical public health concern (3). Non-medical use of prescription drugs (NMUPD) has been defined as the use of a prescription drug i) without a doctor's prescription, ii) for a longer period than prescribed, iii) for other reasons than those for which it was prescribed, or iv) in doses higher than those recommended (3–5). The purpose of use can be recreational (getting high, euphoric or intoxicated) or self-medication (5–7). Most studies took place in the U.S., and no comparison with other drug use has been investigated. The current study compared NMUPD and illicit street drugs in Switzerland.

NMUPD is of growing concern for several reasons. First, NMUPD has been shown in the U.S. to be the the second most common type of drug use after marijuana among teenagers and young adults (8–10). Second, NMUPD is increasing, particularly among young populations (11). For example, NMUPD increased by 67% in the U.S. between 1991–1992 and 2001–2002 (12), and is growing faster than marijuana use (10, 13). Thus, NMUPD did not seem to be used only among heavy substance users. Third, prescription drugs are easier to obtain than illicit street drugs (14, 15). People also tend to think that prescription drugs are safer than illicit street drugs (7, 14, 16). However, many studies that looked at the association between NMUPD and mood or personality disorders showed that NMUPD is associated

with detrimental effects, such as cognitive deficit and mood disorders (e.g., depression, accidental overdoses, and psychiatric disorders) as well as physical problems (e.g., organ damage), and other substance use disorders (2, 12, 15–22). These results seemed to be inconsistent with the belief that NMUPD are safer than illicit street drugs and that prescription drugs are not "really drugs" (23). However, no study has yet to compare the respective associations between NMUPD and illicit street drugs on the one hand and mental health issues on the other hand.

Therefore, the aim of this study was to investigate the relationship between drug use (illicit street drugs and NMUPD) and mental health issues (depression and mental health problems, i.e., sadness, nervousness, and depression). We aimed to find out which association was higher. A total of 16 illicit street drugs, including cannabis, and five types of NMUPD (sleeping pills, sedatives, pain killers, antidepressants, and stimulants) were analyzed. Moreover, this study aimed to provide further insights regarding NMUPD in another country (Switzerland) than the U.S. and Canada, where most previous studies have been conducted (15).

Materials and methods

Sample and data collection

The data used in this study form part of the Cohort Study on Substance Use Risk Factors (C-SURF). C-SURF is a longitudinal study, which is taking place in Switzerland and is designed to assess substance use patterns and related consequences in Swiss young men. Illicit drug use, NMUPD, and mental health issues were collected at the same time during the baseline assessment of the C-SURF study. Enrolment took place between August 23, 2010 and November 15, 2011 at three (of six) army recruitment centers located in Lausanne (French-speaking) and Windisch and Mels (German-speaking). These centers cover 21 of 26 cantons in Switzerland, including all French-speaking cantons. In Switzerland, army recruitment is mandatory, so the study was largely representative of all young Swiss men. The study obtained ethical approval by the Ethics Committee for Clinical Research of the Lausanne University Medical School and followed the Helsinki declaration.

Altogether, of the 13,245 conscripts informed about the study, 7563 gave written consent to participate and 5990 filled in the baseline questionnaire. Missing values were listwise deleted, so the study ultimately included 5719 participants (95.5% of the sample). More information about sampling and non-response can be found in Studer et al. (24). Non-respondents were more often substance users, but the differences between respondents and non-respondents were small and may be significant only because of the large sample size.

Measures

Participants who consented to participate were invited by mail or email to fill in a paper and pen or an online questionnaire, according to the preference they indicated in the written consent. The questionnaire lasted approximately 1 h and included topics such as sociodemographic background, health, family background, substance use (alcohol, tobacco, cannabis, other illicit drugs, NMUPD), personality and leisure time activities, and sexuality. Participants answered first health issues, followed by questions on substance use.

NMUPD

NMUPD was assessed with five questions about the use of prescription drugs without a doctor's prescription or for reasons other than those indicated during the past 12 months. The answers were collected on an 8-point scale (never, once, 2–3 times a year, 4–9 times a year, 1–2 times a month, 3–4 times a month, 2–3 times a week, and 4 times a week or more) and coded dichotomously as "used" or "not used". The prescription drugs and associated examples were as follows: i) sleeping pills (e.g., benzodiazepine (Dalmadorm®, Rohypnol®, Halcion®), barbiturate, chloralhydrate (Nervifène®), zopiclon, zolpidem (Imovane®, Stilnox®)); ii) tranquilizers (e.g., benzodiazepine (Valium®, Xanax®, Librax®, Temesta®, Normison®, Demetrin®, Dalmadorm®) and muscle relaxing drugs); iii) strong painkillers (e.g., buprenorphine (Tamgesic®), codeine (Benylin®), opium-based products (Fentanyl®, Hydrocodon®, Jurnista®, Palladon®, Targin®, Oxycontin®, Vicodin®, Dilaudid®) and DXM (Bexin®), but over-the-counter painkillers such as Aspirin® and Paracetamol® were excluded); iv) antidepressants (Remeron®, Fluoxetine®, Citalopram®, Trimin®); and v) stimulants (e.g. amphetaminsulphate (Aderall®), atomoxetine (Strattera®), methylphenidate (Ritalin®)).

Illicit street drugs

The prevalence rate of illicit street drugs during the past 12 months was measured for 16 drugs. The drugs were as follows: i) cannabis (hashish, marihuana, grass); ii) hallucinogens, magic mushrooms, psilocybin, peyote, mescaline; iii) other hallucinogens (LSD, PCP/Angeldust, 2-CB, 2-CI); iv) salvia divinorum; v) speed; vi) amphetamine, methamphetamine, amphetaminsulfate (e.g., Dexedrine, Benzedrin); vii) crystal meth (Ice); viii) poppers (Amylnitrit, Butylnitrit); ix) solvent sniffing (e.g., glue, solvent and gas such as benzin, ether, toulol, trichloräthylen, nitrous oxide); x) ecstasy, MDMA; xi) cocaine, crack, freebase; xii) heroin; xiii) ketamine (Special K), DXM; xiv) GHB/GBL/I-4 Butandiol (BDB); xv) chemicals used in research (e.g., mephedrone, butylone and methedrone); and xvi) spices or similar substances (synthetic marijuana). The drugs were aggregated into five subclasses: 1) cannabis; 2) hallucinogens, including magic mushrooms, other hallucinogens, salvia divinorum and spice; 3) uppers, including speed, ecstasy, cocaine and amphetamine; 4) sniffed drugs, including poppers and solvents; and 5) "hard" drugs, including crystal meth, heroin, ketamine and chemicals used in research. Each subclass was collected on a 3-point scale (never, 1–3 times, 4 times or more) and coded dichotomously "used" or "non-used". Participants indicated first their illicit street drug use, and then their NMUPD.

Mental health issues

Mental health issues were assessed with depression and mental health problems. The Major (ICD-10) Depressive Inventory (WHO-MDI) was used to determine the level of depression (25, 26). It comprises 10 criteria, with two criteria being assessed by two questions (restless vs. subdued and increased vs. reduced appetite, where the higher score of the two alternatives for each criterion was used). A six-point scale ranging from "never" (0) to "all the time" (5) was used, and a total score from 0 to 30 was computed (Cronbach's α=0.91). Mental health was assessed with six questions from the 12-item Short-Form Health Survey (SF-12) [SF-12; (27)], which deals with sadness, nervousness, and depression. The total score was computed according to the authors' recommendations (with a standardized mean of 50, wherein the lower values reflect bad mental health, Cronbach's α=0.61). Participants were asked to complete SF12 first, and then WHO-MDI.

Covariates

Demographic covariates included language (French- or German-speaking), urbanicity (urban area: more than 10,000 inhabitants; rural area: <10,000 inhabitants), perceived family income ("below-average income", "average income", "above-average income") and completed education (primary: 9 years of schooling; secondary: around 12 years; tertiary: 13 years or more, including university).

Statistical analyses

First, descriptive statistics were computed to investigate the prevalence rate of NMUPD. Linear regressions were then performed to test the relationship between drug use and mental health issues, comparing illicit street drugs and NMUPD's associations with mental health issues. Depression and mental health were successively considered as outcome variables, while illicit street drug and NMUPD were considered dichotomic exposure variables. Simple linear regressions were performed for each of the five subclasses if illicit street drugs and five NMUPD for the two outcome variables. Multiple linear regressions, including all the illicit and NMUPD, were performed for the two outcome variables. Multicollinearity was checked to avoid reducing the predictive power of the model. Simple and multiple regressions were performed to test the individual and combined influence of each drug on mental health as well as to isolate the relationship between each drug used and mental health, accounting for the other drugs. Indeed, one can suppose that the drugs share common variance and this covariance should be taken into account to properly reflect the relationship between drug use and mental health. All the models were tested with adjustment for demographic variables (adjusted models). Standardized regression slopes (β) were presented instead of raw slopes to permit comparability between different drugs (illicit street drugs and NMUPD) with a scale-free estimation (28). The standardized slope could be considered as an effect-size index (28). A Bonferroni-Holms correction was performed in post-hoc comparisons to keep the type I error rate at 5%. All the analyses were conducted with SPSS 20.

Results

Preliminary results

The participants' mean age was 20.0 years (SD: 1.23), 55.0% were French-speaking and 41.1% lived in urban areas. Most participants had completed primary education (48.4%, secondary: 26.0%; tertiary or higher: 25.5%) and only 14.3% had a family income below average (average: 41.5%; above average: 44.1%). The average level of depression was low (mean=7.0, SD=7.2) as the average level of mental health problems (mean=47.4, SD=9.1).

The prevalence rates of drug use are illustrated in Table 1. The most prevalent illicit street drugs were cannabis (30.3%), followed by uppers (5.6%) and hallucinogens (5.0%). The most prevalent non-medical prescription drugs were painkillers (6.8%), followed by sleeping pills (3.0%) and anxiolytics (2.6%). Stimulants and antidepressants were less prevalent at rates of 1.9% and 0.9%, respectively.

Associations of mental health issues with NMUPD and illicit street drugs

The simple regressions showed that all the drugs were significantly associated with mental health issues (Table 2). The use of the drug considered during the past 12 months was associated with poorer mental health (for increased depression, coefficients ranged between 0.080 and 0.163, while for decreased mental health, coefficients ranged between −0.056 and −0.131).

In multiple regressions, the comparisons showed that cannabis, sleeping pills, painkillers, antidepressants,

Table 1 Prevalence rates of illicit street drug and NMUPD use during the past 12 months.

	% of users
Illicit street drugs	
Cannabis	30.5
Hallucinogens	5.0
"Hard" drugs	1.2
Sniffed drugs	4.2
Uppers	5.6
Non-medical use of prescription drugs	
Antidepressants	0.9
Anxiolytics	2.6
Painkillers	6.8
Sleeping pills	3.0
Stimulants	1.9

Table 2 Simple linear regressions of mental health (depression and SF12) on illicit drugs (illicit street drugs and NMUPD).

Variables	Depression		SF12	
	β	p-Value	β	p-Value
Illicit street drugs				
Cannabis	0.114	0.000	−0.116	0.000
Hallucinogens	0.111	0.000	−0.078	0.000
"Hard" drugs	0.125	0.000	−0.067	0.000
Sniffed drugs	0.080	0.000	−0.056	0.000
Uppers	0.107	0.000	−0.092	0.000
NMUPD				
Antidepressants	0.159	0.000	−0.108	0.000
Anxiolytics	0.162	0.000	−0.101	0.000
Painkillers	0.126	0.000	−0.086	0.000
Sleeping pills	0.163	0.000	−0.131	0.000
Stimulants	0.123	0.000	−0.076	0.000

Notes: Adjusted standardized slopes (β), β standard errors (SE) and p-value (p) are given. A Bonferroni-Holm correction was applied.

and anxiolytics were significantly associated with mental health issues (except for anxiolytics with SF12), whereas other illicit street drugs were never significantly associated with mental health issues (Table 3). Participants who reported higher levels of depression or mental health problems were more likely to be cannabis and non-medical prescription drug users, with the exception of stimulants, which were not associated with mental health. Mental health was not significantly associated with any other illicit street drug.

Table 3 Multiple linear regressions of mental health (depression and SF12) on illicit drugs (illicit street drugs and NMUPD).

Variables	Depression		SF12	
	β	p-Value	β	p-Value
Illicit street drugs				
Cannabis	0.080	0.000	−0.093	0.000
Hallucinogens	0.026	0.082	−0.005	0.759
"Hard" drugs	0.036	0.060	0.004	0.772
Sniffed drugs	0.022	0.098	−0.015	0.276
Uppers	0.000	0.994	−0.027	0.080
Non-medical use of prescription drugs				
Antidepressants	0.073	0.000	−0.052	0.000
Anxiolytics	0.073	0.000	−0.035	0.084
Painkillers	0.056	0.001	−0.040	0.021
Sleeping pills	0.078	0.000	−0.080	0.000
Stimulants	0.028	0.176	−0.006	0.684

Notes: Adjusted standardized slopes (β) and p-value (p) are given. A Bonferroni-Holm correction was applied.

Discussion

Main findings

This study compared the associations of NMUPD and illicit street drug use with mental health issues (depression and mental health problems) within a sample of young Swiss men. It also attempted to determine whether one of these two kinds of drugs was associated with increased mental health issues. The study also provided further insights regarding NMUPD in countries other than the U.S. and Canada, where NMUPD has been most studied.

The prevalence rate for NMUPD and illicit street drug use during the previous 12 months indicated that cannabis was, by far, the most common drug used by the participants (30.3%). The second most used substance was painkillers (6.8%). This result is in accordance with previous studies that reported painkillers to be the most common NMUPD (15, 29–31), after cannabis use. The new epidemic observed in North America may then also affect Switzerland. Calming prescription drugs were more prevalent than stimulants (sleeping pills: 3.0%, anxiolytics: 2.6%), as was found in the U.S. in the "Monitoring the Future" study (31). By contrast, the most prevalent illicit street drugs other than cannabis were stimulants (5.6%) and hallucinogens (5.0%). Downers seemed to be more popular among prescription drugs and uppers among illicit street drugs.

Mental health issues were found to be differently associated with drug use when simple or multiple regressions were performed. In simple regression, the use of each substance was associated with poorer mental health. However, when multiple regressions were performed, the only significant associations were for cannabis and NMUPD (except stimulants for depression and SF12, and anxiolytics for SF12). Cannabis use and NMUPD were associated with higher levels of mental health problems and depression than non-cannabis use or non-NMUPD. This means that the illicit street drugs other than cannabis and prescription stimulants showed no detrimental associations with mental health when their common variance with cannabis and NMUPD was eliminated. Even if illicit drugs other than cannabis were individually associated with poorer mental health, when all the substances were combined, cannabis and NMUPD were sufficient in explaining the relationship between drug use and mental health. This was due to the fact that the remaining and proper variance of illicit drugs other than cannabis was not significantly associated with mental health issues. The result was true even for the "hardest" illicit street

drugs, including heroin, ketamine or crystal meth. Users think that prescription drugs are safer than illicit street drugs (7, 14, 16). In relation to this, the results highlighted in this study showed that it was not the case. Interestingly, prescription stimulants showed a similar pattern as illicit street drugs, thus suggesting that prescription stimulants should be used similarly as illicit street drugs, whereas downers NMUPD were not. This could be because prescription stimulants and illicit street drugs were used to get high and for recreational purposes, whereas downers NMUPD were used for the purpose of coping. However, more studies are needed, as motives of use were not investigated in the current study. Finally. cannabis was the only illicit street drug that showed significant associations with mental health issue. Previous findings showed that cannabis is harmful to health (32), and the result of this study, even if it did not access a causal relationship between cannabis use and mental health, is especially worrying given that cannabis is the most used illicit drug worldwide (33, 34).

Limitations

This study presents several limitations. The most critical is that this cross-sectional study did not allow the determination of causality, that is, whether NMUPD is a cause or a consequence of mental health issues This is a common limitation in studies on drug use (5, 16, 35). For example, antidepressants may be overused by people who are already depressed, so NMUPD may be a consequence of depression and not a cause. However, irregular use of antidepressants is also associated with worsening depression (36, 37). Another limitation is the similarity between mental health issues and intoxication symptoms. Indeed, many symptoms of intoxication resemble the symptoms of mood disorders (8). Thus, it can be difficult to distinguish between "real" mental health issues and the effects of heavy use of non-medical prescription drugs. Nevertheless, the participants in our study were not heavy users.

Regarding stimulants, both illicit street drugs and prescription stimulants included similar components (for example, Dexedrine). Therefore, confusion may have occurred for these two subclasses of substances.

We do not know whether prescription drugs were used by our participants to get high or as self-medication. Thus, further research is needed to highlight the prevalence rate and effect of NMUPD in relation to reasons for this use, as well as to investigate the difference between downer prescription drugs and prescription stimulants. Finally, the study focused exclusively on young Swiss men and is not representative of the general population. However, sex effects on NMUPD are well documented (3, 12, 15, 16, 18, 21) and the enrolment procedure in army centers enables a representative sample not exclusively composed of college or high school students.

Conclusion

This study indicated that NMUPD could be just as worrying as illicit street drug use. Indeed, NMUPD not only shows a high and increasing occurrence in Western countries, it is also strongly associated with mental health issues and such associations outstripped those of mental health issues with illicit street drugs. The findings supported the idea that NMUPD are not "safe drugs", and preventive information and interventions may focus on this class of drugs, especially for NMUPDs that are highly addictive (opiates and sleeping pills).

Conflict of interest statement

Authors' conflict of interest disclosure: none.
Source of funding: Swiss National Science Foundation FN 33CS30_139467.

Received September 23, 2013; accepted November 28, 2013; previously published online January 22, 2014

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